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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/987,930	11/16/2001	Thomas P. Jerussi	4821-438-999	7891

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EXAMINER	
KIM, VICKIE Y	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 03/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/987,930	JERUSSI ET AL.	
	Examiner	Art Unit	
	Vickie Kim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-15 and 58-78* is/are pending in the application.

4a) Of the above claim(s) *60,68 and 70-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-15,58,59,61-67,69, 76-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RCE acknowledged

A request for continued examination(RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/23/05 has been entered.

Status of Application

1. Acknowledgement is made of amendment filed 8/23/05. Upon entering the amendment, the claims 13, 15, 58 are amended. New claims 61-78 are added.

2. Acknowledgement is made of Affidavits filed 8/23/05. They are carefully considered and put on the record.

Election acknowledged

3. Applicants' election of species, the compound (2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and anxiety disorder are acknowledged. Applicants traverse the election requirement on the grounds that there would be no burden in searching the entire genus. This argument is not persuasive, as not all invention/species encompassed by the genus would be classified together. Furthermore, even if there

were unity of classification, the search of the entire genus in the non-patent(a significant part of a thorough examination) would be burdensome. Therefore, the election requirement is maintained, and made FINAL.

4. Claims 13-15, 58-78 are now pending. The elected claims 13-15, 58-59, 61-67, and 69 have been examined only to the extent that they read on use of the elected species in the claimed method. All remaining(or portions thereof) not drawn to the elected species are withdrawn from further consideration as being non-elected. The following rejections are made.

Claim Rejections - 35 USC § 112, 1st

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

1. claims 13-15, 58-59, 61-67, and 69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims because the specification, while being enabling for TREATING or reducing the occurrence of affective disorder(e.g. anxiety disorder) in a patient in need thereof, does not reasonably provide enablement for preventing said affective disorders as claimed in claim 13 using a drug claimed.

Attention is directed to In re Wands, 8 USPQ 1400 (CAFC 1988) at 1404 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls) at 547 the court recited eight factors:

1) *The nature of the invention:*

The instant invention is drawn to a treatment of anxiety disorder using an effective amount of bupropion metabolite(i.e. (2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol as claimed in claim 15.

2) *The state of the prior art:*

As the state of art recognizes, there are numerous path-etiologic factors(e.g.bio-pathways and pathogens) involved in developing such neurological disorders as claimed and not fully understood yet.

The state of the art recognizes that the significance of particular drug treatment for modifying different aspects of biological activity cannot be predicted a priori and furthermore, the treatment of bupropion metabolite may not be significantly altering or influencing all the possible path-etiologic factors.

The state of the art also recognizes that a single drug treatment can not be effectively treating all the claimed diseases where complexed etiologic factors are involved in different level and strength. And thus, a

single drug therapy is selectively effective and used in the treatment of the specific condition(s) but not for all the claimed diseases .

3) *The relative skill of those in the art:*

The relative skill of the those in the art is high.

4) *The predictability of the art:*

The high degree of **unpredictability** in pharmacological activity in general and the drug treatment is well known in the art. A slight change in the structure of the drug would drastically change its influence on receptor binding activity and selectivity. Note that in cases involving physiological activity such as the instant case, " the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F 2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

For a pharmaceutical composition containing multiple active ingredients or carriers having different chemical structures and modes of actions, their interaction, co-action, e.g. synergism etc. is even more unpredictable. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds in the treatment of all the claimed conditions.

5) *The breadth of the claims:*

i. Applicant's assertion that the inventive compounds and its composition would be useful for preventing anxiety completely does not

commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability without working examples. It is noted that However, the claims must be given their broadest reasonable interpretation. Therefore, the interpretation of claims (i.e. prevention of affective diseases) should be made based on the full definition of the term "prevention" including "forestall affective disease completely" wherein the claims become not enabled.

6) *The amount of guidance/working examples:*

An extensive research investigation is made into various diseases and conditions as claimed caused by numerous patho-etiologic factors (not fully understood) in the human body as it interplays with nutrition, genetics, Stress and impaired immunity and the complex factors which are normally responsible for the outbreaks of such conditions and diseases. Furthermore, the present invention deals with various conditions and diseases which are not classified together nor have same manifestations.

With lack of evidentiary support, it is beyond the skill of skilled artisan today to get an agent to prevent all the claimed conditions(e.g. anxiety) completely.

The specification provides lack of evidential support substantially where any skilled artisan can not clearly understand how the claimed invention(i.e. a method of treating diseases as claimed) is made and used

at the time of the invention with the information provided and thus, the claims are considered not enabled with the information given.

7) *Quantitation of undue experimentation.*

Since insufficient teaching and guidance have been provided in the specification, one of ordinary skill in the art, even with high degree of skill, would not be able to use the composition as claimed without undue experimentation except for treating affective disorders in need thereof using the invention composition containing bupropion metabolite.

The true fact of the state of the art in cancer therapy is expressed well, "The significance of particular drug treatment for modifying different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study " to determine the efficacy against all the diseases as claimed.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 13-15, 58-59, 61-67, and 69 are rejected under 35 U.S.C. 102(e) as being anticipated by Morgan (US6391875, 6274579, 2003/0064988) in view of Young(US2003/0022942).

*** Note: all these patents are children cases of US6274579, and disclosures therein are substantially same. Therefore, the examiner will use US'579 to represent all these cases.

The claims are drawn to a method of treating or preventing an affective disorders (e.g. anxiety disorder) by administering a therapeutically or prophylactically effective amount of (2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (or salt, salvates thereof) as a bupropion metabolite.

Morgan et al(US'579) teaches a compound (2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and its composition used for various psychogenic disorders such as depression or addiction, see abstract and col.2, lines 21-63 and col.5, lines 36-52.

Claims differ because they are drawn to a method of treating or preventing anxiety.

However, it would have been obvious to one of ordinary skill in the art at that time of the invention was made to employee bupropion metabolite(i.e. 2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol) to treat anxiety when Morgan's patent is taken in view of Young(US'942) because Young teaches that bupropion is effectively used in the treatment of anxiety, see paragraph 13.

One would have motivated to use bupropion metabolite(US'579) to treat anxiety, with reasonable expectation of success, because bupropion and its metabolites utilizese same pathway and should obtain same pharmacological effectiveness against anxiety treatment.

One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities, and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

The effective dosage regimen(see col.5, lines 40-45), formulations(from col.5, lines 63 to col.6, lines25) and routes of administration(col.5, lines 59-62) are well taught and thus, the dependent claims 61-67 are properly included in this rejection.

US579 also teaches pure enantiomers and racemates, see col 3, lines 10-15.

Young(US'942) also teaches optically pure isomer of bupropion, see paragraph 28. At paragraphs 31 and 36, Young teaches disadvantages of racemic mixture of bupropion and advantage of using pure isomer to reduce side effect associated with racemic mixture. Thus, claim 59 are met and included in this rejection.

Conclusion

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this inal action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 571-272-0579. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris Low be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

VICKIE KIM
PRIMARY EXAMINER

Vickie Kim/
Primary Patent Examiner
February 21, 2006
Art unit 1618